

In the Specification

Please amend the paragraph at page 25, lines 13- 24 as follows:

Expression of the ER stress inducible proteins including CHOP/Gadd153 and ATF-6 was induced in syno^{-/-} MEFs described above (data not shown). These proteins are considered to be involved in [[UPR]]UPR against ER stress. Therefore, in syno^{-/-} MEFs, apoptosis was thought to be induced not through the UPR system responding to ER stress, but by the breakdown of ERAD system. Namely, the ERAD system seems to be mainly involved in the quality control of proteins and it is at the same time indispensable for the ‘maintenance of life,’ especially during processes of embryonic development. Several ubiquitin ligases (E3) such as CHIP, gp78/AMFR, Parkin, and Fbx2/FBG1/NFB42 have been reported to be involved in the ERAD system. However, synoviolin’s ‘loss-of-function’ causes lethality during embryonic development processes since no substitutive function is available. Our study clearly suggests that synoviolin among other ubiquitin ligases (E3) plays a pivotal role in the ERAD system, in particular.